REMARKS

Claims 97, 157 through 176 are under examination in the application.

Claims 166 through 170, 172 and 173 are amended herein to recite "microarray" or "microarrays" rather than simply "array" or "arrays." The specification does not expressly disclose either "microarray" or "microarrays" but the disclosure is inherent in the application as filed, for example, in original claims 49 and 64, each reciting microchips comprising an array of oligonucleotide, page 17, line 12, describing probes preferably fixed in an array on a microchip, and page 23, lines 22 through 24, teaching probes fixed in a square array on a microchip which may be in the range of 1 mm^2 or 1 cm^2, each of these disclosure clearly teaching the arrays to be subcomponents on a microchip, thereby teaching that the arrays themselves are at least micro in scale. The amendment therefore includes not new matter.

Claims 97, 157 through 161, and 166 through 171 were rejected under 35 USC §102(b) for being directed to subject matter assertedly anticipated by the disclosure of US Patent No. 4777020 ("the '020 patent").

Claims 162 and 172 were rejected under 35 USC §103(a) for being directed to subject matter assertedly rendered obvious by the disclosure of the '020 patent in view of the disclosure of US Patent No. 4981783 ("the '783 patent").

Claims 163 through 165 and 173 through 175 were also rejected under 35 USC §103(a) for reciting subject matter assertedly rendered obvious by the disclosure of the '020 patent in view of the disclosure of Southern et al., Genomics (1992) 13:1008-1017 ("Southern").

A notice of appeal accompanies this submission.

The rejection under 102(b)

The examiner rejected claims 97, 157 through 161, and 166 through 171 under 35 USC §102(b) for being directed to subject matter assertedly anticipated by the disclosure of the '020 patent. Referring to disclosure at col. 8, lines 1 through 55, and Figure 6, the

examiner specifically asserted that the '020 patent anticipates the subject matter of claims 97 and 166 in disclosing a support comprising an array of microchips on the support, each of the microchips comprising an array of oligonucleotide probes, each of the microchips separated by a physical barrier and each of the microchips having oligonucleotides of different sequences attached to different locations (i.e., polynucleotides are separated by length via electrophoresis gel and blotted onto slides. Regarding claims 157 and 168, the examiner asserted the patent discloses a space between opposing slides in the disclosed device thereby providing a groove along the edge between the slides. Regarding the subject matter of claims 158 and 169, the examiner asserted the patent discloses adjacent slides separated by silicone shims. Regarding claims 159 and 169, the examiner asserted that the patent discloses the support comprises rows and columns, i.e., 30 slide pairs inserted into a holder providing two rows of 30 columns. Regarding claims 160 and 170, the patent is purported to disclose multiple slide pairs arranged in the slide holder to form a gap between the surfaces of the slide pairs for sample application using a pipette. Regarding these same claims, the examiner alleged that the phrase "for use with a multichannel pipette "does not further limit the invention. Finally, regarding the subject matter of claims 161 and 171, the examiner asserted the '020 patent discloses "the device wherein the device comprises assay ingredients, e.g., labeled sample" at col. 10, lines 8 through 15..

The applicants respectfully traverse, submitting that the examiner's position is incorrect from a factual standpoint and therefore cannot be sustained.

In rejecting the subject matter of claims 97 and 166, the examiner specifically relied on disclosure in the '020 patent of an assembly of two microscope slides (610 and 630 in Figure 6A), the two slides in a flat "stacked" position relative to each other, with the opposing flat surfaces between the two slides separated by a gap maintained by the positioning of each slide in a slot (158) in a single slide holder (156). On one flat surface of each slide (those sides of the two slides that are facing each other across the gap) is a membrane filter material (623 and 643). On each slide, between the membrane material and the slide holder is a coating (622 and 642). The patent teaches that the membrane materials can be "spotted directly with samples" such as cells or cellular extracts of protein or DNA (Col. 8, lines ~ 37 through 39) in dotting assays, or in blotting assays wherein the membranes are "blotted against an electrophoretic gel or other separating device so as to transfer

previously separated species" such as antigens or polynucleotides in a "defined spatial relationship." (Col. 8, lines ~ 46 through 50) Given that the examiner is equating the gap between the two slides, and/or the coating on each slide with the recited physical barrier, at best the disclosure in the '020 patent can be analogized to two arrays or two microchips separated by a barrier. This disclosure, however, is distinct from the subject matter of claims 97 and 166 for several reasons.

Broad claims 97 and 166 recite the terms "array" and "microarray" Specifically, claim 97 recites, *inter alia*, a support comprising an array of microchips immobilized on said support, each of said microchips comprising an array of oligonucleotide and said microchips being separated by a physical barrier or a hydrophobic surface. Here, the product includes arrays of arrays. Likewise, claim 166 recites, *inter alia*, an array of microarrays of oligonucleotides, said oligonucleotides immobilized on said support, wherein each microarray is separated by a physical barrier or a hydrophobic surface from every other array. Thus, in order for the '020 patent to anticipate the subject matter of these claims, some aspect of the '020 patent disclosure must be construed by the examiner as (i) a multiplicity of microarrays of oligonucleotides as required by claim 166, each array separated from each other by some type of physical barrier and (ii) a multiplicity of oligonucleotide arrays on a multiplicity of arrayed microchips as required by claim 97, wherein each microchip is separated from each other microchip by some type of physical barrier. The difference between the two claims is that in claim 97, oligonucleotides are immobilized on microchips which are arrayed on the support, and in claim 166, oligonucleotides are immobilized directly on a support and arrayed in individual arrays.

The cited art does not disclose a microchip or a microarray

Regarding the subject matter of claim 97, the examiner failed to point to any teaching in the '020 patent which can reasonably be interpreted to be a microchip. MPEP 2111, citing *Phillips v. AWH Corp.*, 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005), advises "The Patent and Trademark Office ("PTO") determines the scope of claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction 'in light of the specification as it would be interpreted by one of ordinary skill in the art.' *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364[, 70

USPQ2d 1827] (Fed. Cir. 2004)." Nothing, however, in the '020 patent teaches or suggests that any part of the disclosure is reasonably contemplated on a micro-scale. Though not limiting to the claimed subject matter, the "micro" scale for the recited chips exemplified throughout the specification is distinct from a slide disclosed in the '020 patent. For example, at page 40, lines 8 through 17, the specification teaches,

> A basic example is using 6-mers attached to 50 micron surfaces to give a chip with dimensions of 3 x 3 mm which can be combined to give an array of 20 x 20 cm. Another example is using 9-mer oligonucleotides attached to 10 x 10 microns surface to create a 9-mer chip, with dimensions of 5 x 5 mm. 4000 units of such chips may be used to create a 30 x 30 cm array. FIG. 2A, FIG. 2B and FIG. 2C illustrate yet another example of an array in which 4,000 to 16,000 oligochips are arranged into a square array.

Similarly, as another example, the entirety of a microchip is exemplified at page 23, lines 22 through 24 in the description wherein "[o]ne set of such probes of length F (4.sup.F) would be fixed in a square array on a microchip--which may be in the range of 1 mm^2 or 1 cm^2." It is noted that the microchip of this invention is analogous to a computer microchip; the computer microchip *per se* is not necessarily micron in scale, but the components thereon are. Here, the oligonucleotide microchips are not themselves necessarily micron scale, but the oligonucleotides placements are. This level of miniaturization is neither disclosed or suggested in the cited patent, and thus, the examiner is invited to explain how, at the time the instant application was filed, one of ordinary skill in the art would interpret the instant micro scale subject matter of the claims to read on the relatively macro scale device in the '020 patent.

In addition, even if one assumes the examiner is correct (and the applicant does not) and the '020 patent discloses arrays of any type, as discussed above, at best the product in Figure 6 can be construed to provide two "arrays" on two separate microscope slides, i.e. "arrays" positioned on two separate supports that are positioned in a single holder. Nothing in the patent discloses or suggests the array of arrays (i.e., array of microchips comprising arrays of oligonucleotides) as required in claim 97, or multiple microarrays as recited in claim 166, both of which are attached to a support. Moreover, in light of the instant specification, the examiner is also invited to explain how one of ordinary skill in the art can construe the instant claims which are exemplified only with essentially two dimensional, or

planar-type, supports to embrace a "stacked slide" device as disclosed in the '020 patent. The applicant fully understands that the "planar" or "essentially two dimension" limitation for a support is not recited in either broad claim, but the issue here is the broadest ***reasonable*** construction of the claims in light of the specification as it would be interpreted by one of ordinary skill in the art. For example, the "planar" aspect is shown in Fig. 2a through 2C, and this planar arrangement is clearly distinct from a stack of slides disclosed in the cited art.

With regard to the specific terms "array" and "microarray" recited in claims 97 and 166, the examiner has not clearly stated where in the '020 patent any disclosure relates to an array as would be interpreted by the same person of ordinary skill in the art in light of the specification. The instant specification does not expressly define the term "array," but implicit meaning can be derived from Figs. 2A, 2B and 2C. Fig. 2A shows "an array of 4^P identical sections each containing identical (or different) arrays of oligonucleotides" wherein "sections can be separated by physical barriers or hydrophobic strips...." (p. 19, lines 3-6) Fig. 2B is an enlargement of a chip section showing the oligonucleotide arrays on the chip. (See p. 19, lines 9-14.) Fig. 2C shows a means to prepare an array from individual oligonucleotide stock solutions. (See p. 19, lines 15-28.) From these disclosures, a minimal definition of an array can be inferred, such as an arrangement of oligonucleotides on a support at identifiable locations. Disclosure in the '783 patent, also relied on by the examiner in the office action and submitted at this point by the applicant to evidence an understanding of the term in the art at the time the instant application was filed, is consistent with this inferred meaning. For example, at col. 3, lines 3-7, the '783 patent discloses,

> Gergen et al (1979) first enunciated the idea that replicas of an arrayed library would be extremely useful. Since the position of each clone in the array is known and reproducible, every time replicas of this are screened with a probe, one accumulates data on each member of the library.

This disclosure in the '783 patent indicates that, not only is the positioning of oligonucleotides known in an array, but also the sequence of the oligonucleotides at each location is known. This definition is consistent with, and generally necessary for, a sequencing use taught in the instant application for the support recited in each of claims 97

and 166; sequence information for a target polynucleotide is derived from its hybridization to a probe of known sequence, and as here, at a known location on the support.

If the examiner is asserting that the membranes 623 and 643 referred to in the '020 patent are either arrays or microchips comprising arrays, the applicant first submits that these components are positioned on separate slides and are therefore not on "a support" as required by both claim 97 and 166. This fact is evidenced by the examiner's assertion that the physical space between the slides corresponds to the recited physical barrier in both claims 97 and 166; a physical space between purported arrays indicates physical separation, thereby requiring separate supports for each alleged array.

However, ignoring the requirement for separate supports for each membrane based on the examiner's interpretation of the '020 patent, it is further submitted that by pointing to this "space," or even the coatings on each slide, as being the recited physical barrier, the examiner is apparently implying that the membranes themselves are equivalent to the arrays of oligonucleotides recited in claim 166 and/or the arrays of microchips recited in claim 97. If this is the examiner's position, the '020 patent at most discloses two asserted arrays, and certainly not arrays of arrayed microchips as recited in claim 97.

If on the other hand, the examiner is asserting that polynucleotide "dots" or gel "blots" as discussed above are the recited arrays or microchips, then this disclosure also fails to anticipate the subject matter of claim 97 or 166 since neither the individual dots nor the individually blotted polynucleotides, regardless of how they are initially separated, are separated on the membranes by the recited physical barrier.

If the examiner is asserting that the coatings (622 and 642) shown in the '020 patent positioned on the same face of the slide as the membrane and at the end of the each slide in the slide holder, correspond to the physical barrier recited in each of claim 97 and 166, nothing in the cited patent indicates that the coating is a physical barrier between arrays or between microchips as defined in the instant specification. For example, the support of both claims includes physical barriers which, as taught in Example III, "keep the chips and the probes in the corresponding arrays" during a hybridization reaction, thereby allowing for separate hybridization reactions to take place on each array on the same support.

However, inasmuch as there is an assertion that this coating is the same as the recited physical barrier of the claims, then it must be the examiner's position that each membrane on each slide face at the opposite end from the coating must be either the microchip of claim 97 or an array of claim 166. Such a position certainly precludes the examiner's assertion that the subject matter of claim 97 and 166 is anticipated; such a position cannot be construed to describe arrays of arrays. That is to say a single array is not an array of arrays.

Inasmuch as all limitations of independent claims 97 and 166 cannot be found in the disclosure of the '020 patent, the rejection of these claims cannot be sustained and must be withdrawn. Moreover, failure by the examiner to demonstrate that the '020 patent disclosure anticipates the independent claims indicates that the examiner has not established that the '020 patent disclosure can anticipate any claims depending from these independent claims which incorporate all limitations of claims 97 and 166. Accordingly, the rejection of all claims under §102 must be withdrawn.

The rejections under 103(a)

Claims 162 and 172 were rejected under 35 USC §103(a) for being directed to subject matter assertedly rendered obvious by the disclosure of the '020 patent in view of the disclosure of the '783 patent. Claims 163 through 165 and 173 through 175 were also rejected under 35 USC §103(a) for reciting subject matter assertedly rendered obvious by the disclosure of the '020 patent in view of the disclosure of Southern.

In view of the discussion above and the showing that the primary reference, the '020 patent, fails to disclose all limitations of the independent claims from which each claim rejected under §103 depends, it necessarily stands that reliance on either of the secondary references for limitations recited only in claims 162 through 165 and 172 through 175 cannot remedy the deficiency in the primary reference. As all limitations are not found in the combined references, and the examiner has not explained why the missing limitations would have been obvious to the person of ordinary skill in the art as mandated by the Supreme Court in *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727 (2007), the applicant submits that the rejection of claims under §103 cannot be sustained and must also be withdrawn.

CONCLUSION

In view of the remarks made herein, the applicant submits that all claims are in condition for allowance and request expedited notification of the same.

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Respectfully submitted,

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